CK

RECEIVED
JUL 27 2004
RANBAXY
I.P. DEPARTMENT

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

RANBAXY LABORATORIES LIMITED
c/o Deshmukh, Jayadeep, R.
Suite 2100
600 College Road East
Princeton, NJ 08540
ETATS-UNIS D'AMERIQUE

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	22.07.2004
Applicant's or agent's file reference: RLL-450WO	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB 03/05331	21.11.2003	21.11.2002

Applicant
RANBAXY LABORATORIES LIMITED et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Hebert, W Tel. +49 89 2399-2152

Form PCT/IPEA/416 (January 2004)

MRL ✓

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference RLL-450WO	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/IB 03/05331	International filing date *(day/month/year)* 21.11.2003	Priority date *(day/month/year)* 21.11.2002
International Patent Classification (IPC) or both national classification and IPC C07D463/00		
Applicant RANBAXY LABORATORIES LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
21.06.2004	22.07.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Bakboord, J Telephone No. +49 89 2399-2168

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IB 03/05331

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-13 as originally filed

Claims, Numbers

1-20 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-20
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-20
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-20
	No:	Claims	

2. Citations and explanations

see separate sheet

V Reasoned statement under Art 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

V.1 The field of the invention relates to monohydrate solvates of loracarbef.

V.2 Reference is made to the following documents:

D1: EP-A-0369686, cited in the application
D2: US-A-4977257, cited in the application
D3: EP-A-0627431
D4: US-A-6001996
D5: EP-A-0439353
D6: US-A-5672700
D7: US-A-5578720

V.3 Novelty

Document D1 discloses a crystalline dihydrate form of loracarbef (claim 1) and a crystalline trihydrate form of loracarbef (claim 5).
Document D2 discloses a crystalline bis N, N'-dimethylformamide solvate of loracarbef (claim 1), a dihydrate mono N,N'-dimethylformamide solvate of loracarbef (claim 3) and a mono N,N'-dimethylformamide solvate of loracarbef (claim 5).
Document D3 discloses a crystalline monohydrate form of loracarbef (claim 1).
Document D4 discloses complexes of loracarbef with parabens (claim 2).
Document D5 discloses a crystalline hydrochloride solvate of loracarbef (claim 1).
Document D6 discloses a crystalline isopropyl alcohol solvate of loracarbef (claim 1).
Document D7 discloses a crystalline hydrochloride ethanol solvate of loracarbef (claim 1), a crystalline hydrochloride methanol solvate of loracarbef (claim 3) and a crystalline hydrochloride propanol solvate of loracarbef (claim 5).

A mono N,N-dimethylacetamide monohydrate solvate of loracarbef is disclosed in none of the documents. Claims 1 and 2 therefore fulfill the requirements of Art 33(2) PCT.

A mono N-methylpyrrolidone monohydrate solvate of loracarbef is disclosed in

none of the documents. Claims 3 and 4 therefore fulfill the requirements of Art 33(2) PCT.

Claims 5, 7-13 describe a process for the preparation of mono N,N-dimethylacetamide monohydrate solvate of loracarbef and are novel by consequence.

Claims 6-13 describe a process for the preparation of mono N-methylpyrrolidone monohydrate solvate of loracarbef and are novel by consequence.

Claims 14, 16-18 describe a process for the preparation of crystalline monohydrate of loracarbef which comprises treating mono N,N-dimethylacetamide monohydrate solvate of loracarbef with acid and are novel by consequence.

Claims 15-18 describe a process for the preparation of crystalline monohydrate of loracarbef which comprises treating mono N-methylpyrrolidone monohydrate solvate of loracarbef with acid and are novel by consequence.

Crystalline monohydrate of loracarbef having a bulk density greater than or equal to 0.6 g/ml is disclosed in none of the documents. Claim 19 therefore fulfills the requirements of Art 33(2) PCT.

Claim 20 describes a pharmaceutical composition comprising a crystalline monohydrate of loracarbef having a bulk density greater than or equal to 0.6 g/ml and is novel by consequence.

V.4 Inventive step

Starting from documents D1-D7 the problem to be solved by the present application may be regarded as how to provide a crystalline form of loracarbef having sufficient density in order to facilitate the formulation of the compounds... The solution of the applicant resides in providing monohydrate solvates of loracarbef. The applicant shows in the examples that the monohydrate solvates of loracarbef of the present application have a bulk density of 0.6 g/ml. As the monohydrate solvates of loracarbef have not been made obvious by the prior art the solution of the applicant may be regarded as involving an inventive step (Art 33(3) PCT.